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AN ABIETANE DITERPENOID FROM *LEONURUS MARRUBIASTRUM*

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Key Word Index—*Leonurus marrubiastrum*; Labiatae; diterpenoid; abietane derivative; leonubiastrin.

Abstract—A new abietane diterpenoid, leonubiastrin, has been isolated from *Leonurus marrubiastrum* and its structure (methyl 6β-acetoxy-7α,11-dihydroxy-3-oxoabieta-1,8,11,13-tetraen-19-oate) established by spectroscopic means. © 1998 Elsevier Science Ltd. All rights reserved

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INTRODUCTION

In continuation of our search for diterpene constituents of Labiatae plants [1–3] we have studied the aerial parts of *Leonurus marrubiastrum*, a species from which several neo-clerodane diterpenoids have previously been isolated [4, 5]. We have isolated a new abietane derivative, leonubiastrin, from an acetone extract of this plant collected in Bulgaria (see Experimental). We report here on the structural elucidation of this compound.

RESULTS AND DISCUSSION

Combustion analysis and low-resolution mass spectrometry indicated the molecular formula $C_{23}H_{28}O_7$ for leonubiastrin (**1**). Its IR spectrum was consistent with the presence of ester (1750, 1730 cm^{-1}), α,β-unsaturated ketone (1660, 1620 cm^{-1}), aromatic (3080, 1580, 1500 cm^{-1}) and hydroxyl (3420 cm^{-1}) groups. UV absorptions at λ_{max} 225 (log ε 4.18) and 284 nm (log ε 3.46) corroborated the presence in **1** of an unsaturated cyclohex-2-enone and a hydroxyphenyl chromophores, respectively [6]. The ^1H NMR and ^{13}C NMR spectra of **1** (Table 1) showed signals for an isopropyl group attached to an aromatic ring, two methyl groups attached to fully substituted sp^3 carbon atoms, two aromatic protons in the *meta*-position (J_m = 1.8 Hz; δ_H 6.61 *d* and 6.84 *d*; δ_C 115.1 *d* and 122.6 *d*), an α,β-unsaturated ketone ($\delta_{H\alpha}$ 6.05 *d*, $\delta_{H\beta}$ 8.32 *d*, J_{vic} = 10.4 Hz; δ_C 197.6 *s*, 125.6 *d* and 159.3

Table 1. ^1H NMR and ^{13}C NMR spectral data for compound **1***

H	**1**	C	**1**
1	8.32 *d*	1	159.3 *d*
2	6.05 *d*	2	125.6 *d*
5α	3.58 *d*	3	197.6 *s*
6α	5.06 *dd*	4	58.3 *s*
7β	4.60 *d*	5	41.9 *d*
12	6.61 *d*	6	73.4 *d*
14	6.84 *d*	7	69.7 *d*
15	2.82 *sept*	8	135.9 *s*
Me-16	1.22 *d*	9	125.3 *s*
Me-17	1.22 *d*	10	40.2 *s*
Me-18	1.63 *s*	11	152.8 *s*
Me-20	1.81 *s*	12	115.1 *d*
6β-OAc	2.03 *s*	13	149.6 *s*
19-COOMe	3.69 *s*	14	122.6 *d*
7α-OH†,‡	2.22 *br*	15	33.4 *d*
11-OH†,‡	5.56 *s*	16	23.7 *q*
$J_{H,H}$ (Hz)		17	23.6 *q*
1,2	10.4	18	18.0 *q*
5α,6α	1.0	19	172.9 *s*
6α,7β	2.2	20	25.6 *q*
12,14	1.8	OAc	170.2 *s*
15,16 (17)	6.9		21.4 *q*
		COO*Me*	53.0 *q*

* Spectra were recorded at 400 MHz (^1H) and 100.6 MHz (^{13}C) in $CDCl_3$. Chemical shifts (δ values) are relative to residual $CHCl_3$ for ^1H (δ_{CHCl_3} 7.25) and to the solvent for ^{13}C (δ_{CDCl_3} 77.00). ^1H NMR spectral parameters were obtained by first-order approximation. All these assignments were in agreement with COSY, HMQC and HMBC spectra.

† These protons were distinguished by NOE experiments.

‡ Disappeared after addition of D_2O.

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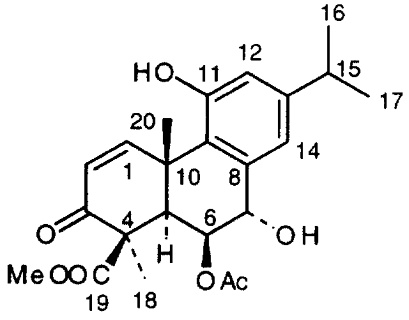
d), a carbomethoxyl group (δ_H 3.69, 3H, *s*; δ_C 172.9 *s* and 53.0 *q*) and an acetoxyl group (δ_H 2.03, 3H, *s*; δ_C 170.2 *s* and 21.4 *q*). In addition, leonubiastrin (**1**) possessed a $(C)_2CH—CHOR—CHOH(C)_2$ structural part (δ_H 3.58 *d*, 5.06 *dd* and 4.60 *d*; δ_C 41.9 *d*, 73.4 *d* and 69.7 *d*). All these functionalities can be accommodated in a structure such as **1** for the new diterpenoid, and this was confirmed as follows.

The chemical shifts and coupling values of the H-1, H-2, H-12, H-14, H-15, Me-16 and Me-17 protons were almost identical to those reported for 11-hydroxyabieta-1,8,11,13-tetraen-3-one [7]. In particular, the downfield resonance of the C-1 proton (δ 8.32) was only compatible [7, 8] with an abieta-1,8,11,13-tetraen-3-one structure possessing a phenol group at the C-11 position, which causes a strong deshielding effect on the C-1 proton due to the close proximity to the oxygen lone pairs of the C-11 hydroxyl group [9]. The ^{1}H NMR pattern showed by the protons at δ 3.58 (1H, *d*, $J = 1.0$ Hz), 5.06 (1H, *dd*, $J = 1.0$ and 2.2 Hz) and 4.60 (1H, *d*, $J = 2.2$ Hz) was attributed to the C-5α, C-6α and C-7β protons, respectively [10]. However, it was the HMBC spectrum of leonubiastrin that provided the most information and established an abietane structure such as **1** for this new diterpenoid, except for its stereochemistry. This spectrum (Table 2) showed correlations between the carboxyl carbon of the acetate (δ 170.2 *s*) and the H-6α proton (δ 5.06 *dd*), thus establishing that the acetate was at the C-6β position. The C-15 methine proton (δ 2.82 *sept*) correlated with the C-16 and C-17 methyl carbons and with three aromatic carbons [δ 149.6 *s* (C-13), 115.1 *d* (C-12) and 122.6 *d* (C-14)], whereas the C-9 carbon (δ 125.3 *s*) showed connectivities with the H-1 (δ 8.32 *d*), H-5α (δ 3.58 *d*), H-7β (δ 4.60 *d*), H-12 (δ 6.61 *d*), H-14 (δ 6.84 *d*), Me-20 (δ 1.81 *s*) and the C-11 phenolic proton (δ 5.56 *s*). These correlations confirmed the partial structure of rings B and C of **1**. Moreover, the carboxyl carbon at δ 172.9 *s* showed connectivity with the methoxyl protons (δ 3.69, 3H, *s*), as well as with the H-5α (δ 3.58 *d*) and the Me-18 protons (δ 1.63 *s*), whereas this last group (Me-18) was correlated with the carbonyl carbon of the α,β-unsaturated ketone (δ 197.6 *s*), thus confirming the partial structure of ring A and establishing that the carbomethoxyl group of **1** must be attached to the C-4 position.

Finally, the stereochemistry depicted in **1** was established from the NOESY spectrum. The axial H-5α proton showed cross-peaks of NOE with the H-6α and Me-18 protons, whereas the pseudoequatorial H-7β proton (see a molecular model of **1**) showed NOE with the H-14 and Me-20 protons. These results were only compatible with the relative stereochemistry shown in **1**.



1

From a biogenetic point of view, it is of interest to note that, to the best of our knowledge, this is the first report on the occurrence of abietanes in *Leonurus marrubiastrum*.

EXPERIMENTAL

General

Mp: uncorr. Plant materials were collected in August 1995, near Samokov, Bulgaria, and voucher specimens were deposited in the Herbarium of the Higher Institute of Agriculture at Plovdiv, Bulgaria.

Extraction and isolation of the diterpenoid

Dried and powdered aerial parts of *Leonurus marrubiastrum* L. (387 g) were extracted with Me_2CO

Table 2. Significant data from the HMBC spectrum of compound 1

C	Correlated with protons	C	Correlated with protons
1	H-5α, Me-20	12	H-14, H-15
2	H-1	13	H-15, Me-16 (Me-17)
3	Me-18	14	H-12, H-15
4	H-2, H-5α, H-6α, Me-18	15	H-12, H-14, Me-16 (Me-17)
5	H-1, H-7β, Me-18, Me-20	16(17)	H-15
6	H-5α	18	H-5α
7	H-6α, H-14	19	H-5α, Me-18, OMe
8	H-6α	20	H-5α
9	H-1, H-5α, H-7β, H-12, H-14, Me-20, OH-11	CH_3COO	H-6α
10	H-1, H-2, H-5α, H-6α, Me-20		
11	H-12, OH-11		

(3×2 l) at room temp. for 7 days. The extracts were evapd *in vacuo* giving a residue (12 g) which was dissolved in 40% aq. Me_2CO (100 ml). This soln was cooled (3–4°) for 24 h and then filtered. This process was repeated for 4×. The combined filtrates were extracted with $CHCl_3$ (4×40 ml) and the organic extracts were dried (Na_2SO_4), filtered and evapd yielding a residue (3.2 g), which was subjected to CC (silica gel Merck No. 7734, deactivated with 10% H_2O, w/v, 100 g) eluting with a petrol–EtOAc gradient (from 100% petrol to 100% EtOAc). Elution with petrol–EtOAc (3:2) gave leonubiastrin (**1**, 52 mg): mp 125–127° decomp. (EtOAc–*n*-hexane); $[\alpha]_D^{20}$ +26.6°, $[\alpha]_{578}^{20}$ +27.2°, $[\alpha]_{546}^{20}$ +28.0°, $[\alpha]_{436}^{20}$ −10.5°, $[\alpha]_{365}^{20}$ −861.2° ($CHCl_3$; *c* 0.353). IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 3080, 1620, 1580, 1500 (aromatic and olefinic), 1750 (COOMe), 1730, 1250 (OAc), 1660 (α,β-unsaturated ketone), 2960, 1435, 1370, 1180, 1140, 1100, 1080, 1070, 1030, 1000, 960, 860: UV λ_{max}^{MeOH} nm ($\log \varepsilon$): 225 (4.18), 284 (3.46). ^1H NMR and ^{13}C NMR: Table 1. EIMS (70 eV, direct inlet) *m/z* (rel. int.): 416 $[M]^+$ (12), 398 $[M-H_2O]^+$ (0.1), 356 $[M-AcOH]^+$ (4), 341 (8), 324 (3), 309 (6), 297 (23), 281 (9), 227 (43), 215 (18), 202 (31), 187 (16), 129 (9), 91 (8), 69 (7), 59 (8), 55 (7), 43 (100), 41 (13). (Found: C, 66.68; H, 6.69. $C_{23}H_{28}O_7$ requires: C, 66.33; H, 6.78%.)

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